```
### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 02.09.15D

Last logoff: 09oct02 12:14:29
Logon file001 09oct02 16:39:55
KWIC is set to 50.
HILIGHT set on as '*'
***                                    ***

File   1:ERIC  1966-2002/Oct 03
       (c) format only 2002 The Dialog Corporation

      Set  Items  Description
      ---  -----  -----------
Cost is in DialUnits
?b 155, 5, 73
       09oct02 16:40:08 User259876 Session D414.1
            $0.30    0.087 DialUnits File1
     $0.30  Estimated cost File1
     $0.04  TELNET
     $0.34  Estimated cost this search
     $0.34  Estimated total session cost   0.087 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2002/Sep W5
*File 155: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File   5:Biosis Previews(R)  1969-2002/Oct W1
         (c) 2002 BIOSIS
*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File  73:EMBASE  1974-2002/Sep W5
         (c) 2002 Elsevier Science B.V.
*File  73: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.

      Set  Items  Description
      ---  -----  -----------
?s (bone (w) marrow (w) stromal (w) cell?) or (MSC?)
Processing
Processing
          962016  BONE
          374796  MARROW
           64045  STROMAL
         7539402  CELL?
            3993  BONE(W)MARROW(W)STROMAL(W)CELL?
            3203  MSC?
     S1     7094  (BONE (W) MARROW (W) STROMAL (W) CELL?) OR (MSC?)
?s s1 (s) ((BMP-2) or (BMP (w) 2))
```

```
            7094  S1
              86  BMP-2
            7797  BMP
         7451944  2
            2258  BMP(W)2
      S2      72  S1 (S) ((BMP-2) OR (BMP (W) 2))
?s s2 and (bone (w) (formation or repair))
              72  S2
          962016  BONE
         1159611  FORMATION
          236099  REPAIR
           28338  BONE(W)(FORMATION OR REPAIR)
      S3      25  S2 AND (BONE (W) (FORMATION OR REPAIR))
?s s3 and (alginate or collagen or polymer)
              25  S3
           11747  ALGINATE
          239662  COLLAGEN
           80771  POLYMER
      S4       9  S3 AND (ALGINATE OR COLLAGEN OR POLYMER)
?s s4 and (adenovirus or adenoviral)
               9  S4
           59014  ADENOVIRUS
           12006  ADENOVIRAL
      S5       3  S4 AND (ADENOVIRUS OR ADENOVIRAL)
?rd
...completed examining records
      S6       1  RD (unique items)
?t s6/3,k/all
```

6/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11180690 21205495 PMID: 11310352

In vitro and in vivo induction of *bone* *formation* using a recombinant *adenoviral* vector carrying the human BMP-2 gene.

Cheng S L; Lou J; Wright N M; Lai C F; Avioli L V; Riew K D
Division of Bone and Mineral Diseases, Dept. of Internal Medicine, Washington University School of Medicine, St. Louis, Missouri, USA.

Calcified tissue international (United States) Feb 2001, 68 (2) p87-94, ISSN 0171-967X Journal Code: 7905481
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

In vitro and in vivo induction of *bone* *formation* using a recombinant *adenoviral* vector carrying the human BMP-2 gene.

It has been well established that bone morphogenetic protein-2 (*BMP*-*2*) can induce *bone* *formation* both in vivo and in vitro, although high concentrations (up to milligrams) of *BMP*-*2* have been required to achieve this effect in vivo. Further, clinical applications are usually limited to a single dose at the time of implantation. In an attempt to prolong the transforming effect of *BMP*-*2* we used a recombinant *adenoviral* vector carrying the human *BMP*-*2* gene (Adv-BMP2) to transduce marrow-derived mesenchymal stem cells (*MSC*) of skeletally mature male New Zealand white rabbits. The pluripotential *MSC* were incubated with Adv-BMP2 overnight followed by culture in growth medium for 1 week. Assays on tissue cultures demonstrated that these Adv-BMP2 transduced *MSC* produced *BMP*-*2* protein, differentiated into an osteoprogenitor line, and induced *bone* *formation* in vitro. These *MSC* had increased alkaline phosphatase activity, increased expression of type I *collagen* , osteopontin, and osteocalcin mRNA, and induced matrix mineralization compared with both non-transduced cells and cells transduced with a control *adenoviral* construct. To analyze the osteogenic potential in vivo, Adv-BMP2-transduced *MSC* were autologously implanted into the intertransverse process space between L5 and L6 of the donor rabbits. The

production of new bone was demonstrated by radiographic...

... weeks later in areas implanted with cells transduced with Adv-BMP2, whereas no bone was evident at sites implanted with cells transduced with the control *adenoviral* construct. Histological examination further confirmed the presence of new *bone* *formation*. These accumulated data indicate that it is possible to successfully transduce mesenchymal stem cells with a recombinant *adenoviral* vector carrying the gene for *BMP*-*2* such that these cells will produce *BMP*-*2*, differentiate into an osteoprogenitor line, and induce *bone* *formation* both in vitro and in vivo. Moreover, incubation of the Adv-BMP2-transduced cells for an additional 7 days in culture before transplantation enhances the success rate in *bone* *formation* (three out of three) as compared with our previous report (one out of five, Calcif Tissue Int 63:357-360, 1998).
...; Bone Marrow Cells--cytology--CY; Bone Marrow Cells--drug effects --DE; Bone Marrow Cells--metabolism--ME; Cell Differentiation --drug effects--DE; Cell Transplantation; Cells, Cultured; *Collagen* --biosynthesis--BI; *Collagen*--genetics--GE; Genetic Vectors; Lumbar Vertebrae--surgery--SU; Models, Animal; Osteocalcin--biosynthesis--BI; Osteocalcin--genetics--GE; RNA, Messenger--metabolism--ME; Rabbits; Sialoglycoproteins--biosynthesis--BI; Sialoglycoproteins...
Chemical Name: Bone Morphogenetic Proteins; Genetic Vectors; RNA, Messenger; Sialoglycoproteins; bone morphogenetic protein 2; Osteocalcin; osteopontin; *Collagen*; Alkaline Phosphatase
?ds

Set	Items	Description
S1	7094	(BONE (W) MARROW (W) STROMAL (W) CELL?) OR (MSC?)
S2	72	S1 (S) ((BMP-2) OR (BMP (W) 2))
S3	25	S2 AND (BONE (W) (FORMATION OR REPAIR))
S4	9	S3 AND (ALGINATE OR COLLAGEN OR POLYMER)
S5	3	S4 AND (ADENOVIRUS OR ADENOVIRAL)
S6	1	RD (unique items)

?rd s4
...completed examining records

S7	4	RD S4 (unique items)

?s s7 not s6

	4	S7
	1	S6
S8	3	S7 NOT S6

?t s8/3,k/all

8/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12710055 21588136 PMID: 11551928
Cloning and characterization of a novel WD-40 repeat protein that dramatically accelerates osteoblastic differentiation.
Gori F; Divieti P; Demay M B
Endocrine Unit, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114, USA.
Journal of biological chemistry (United States) Dec 7 2001, 276 (49) p46515-22, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: 1 F32 DE-05754; DE; NIDCR; 1 KO8 DK02889; DK; NIDDK; DK36597; DK; NIDDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The bone morphogenetic proteins (BMPs) play a pivotal role in endochondral *bone* *formation* . Using differential display polymerase chain reaction, we have identified a novel gene, named BIG-3 (*BMP*-*2* -induced gene 3 kb), that is induced as a murine prechondroblastic cell line, MLB13MYC clone 17, acquires osteoblastic features in response to *BMP*-*2* treatment. The 3-kilobase mRNA encodes a 34-kDa protein

containing seven WD-40 repeats. Northern and Western analyses demonstrated that BIG-3 mRNA and protein were induced after 24 h of *BMP*-*2* treatment. BIG-3 mRNA was expressed in conditionally immortalized murine *bone* *marrow* *stromal* *cells* , osteoblasts, osteocytes, and growth plate chondrocytes, as well as in primary calvarial osteoblasts. Immunohistochemistry demonstrated that BIG-3 was expressed in the osteoblasts of calvariae...

...clones. This increase in cAMP production was associated with an increase in PTH binding. Expression of BIG-3 increased mRNA levels encoding Cbfa1, type I *collagen*, and osteocalcin and accelerated formation of mineralized nodules. In conclusion, we have identified a novel WD-40 protein, induced by *BMP*-*2* treatment, that dramatically accelerates the program of osteoblastic differentiation in stably transfected MC3T3E1 cells.

8/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11282430 21348043 PMID: 11455579

Estrogen modulates estrogen receptor alpha and beta expression, osteogenic activity, and apoptosis in mesenchymal stem cells (MSCs) of osteoporotic mice.

Zhou S; Zilberman Y; Wassermann K; Bain S D; Sadovsky Y; Gazit D
Molecular Pathology Laboratory, Hebrew University-Hadassah Medical and Gene Therapy Center, Jerusalem 91120, Israel.

Journal of cellular biochemistry (United States) 2001, Suppl 36 p144-55, ISSN 0730-2312 Journal Code: 8205768
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

...mouse, ovariectomy (OVX) leads to significant reductions in cancellous bone volume while estrogen (17beta-estradiol, E2) replacement not only prevents bone loss but can increase *bone* *formation*. As the E2-dependent increase in *bone* *formation* would require the proliferation and differentiation of osteoblast precursors, we hypothesized that E2 regulates mesenchymal stem cells (*MSCs*) activity in mouse bone marrow. We therefore investigated proliferation, differentiation, apoptosis, and estrogen receptor (ER) alpha and beta expression of primary culture *MSCs* isolated from OVX and sham-operated mice. *MSCs*, treated in vitro with 10(-7) M E2, displayed a significant increase in ERalpha mRNA and protein expression as well as alkaline phosphatase (ALP) activity...

... mRNA and protein expression as well as apoptosis in both OVX and sham mice. E2 up-regulated the mRNA expression of osteogenic genes for ALP, *collagen* I, TGF-beta1, *BMP*-*2*, and cbfa1 in *MSCs*. In a comparison of the relative mRNA expression and protein levels for two ER isoforms, ERalpha was the predominant form expressed in *MSCs* obtained from both OVX and sham-operated mice. Cumulatively, these results indicate that estrogen in vitro directly augments the proliferation and differentiation, ERalpha expression, osteogenic gene expression and, inhibits apoptosis and ERbeta expression in *MSCs* obtained from OVX and sham-operated mice. Co-expression of ERalpha, but not ERbeta, and osteogenic differentiation markers might indicate that ERalpha function as an activator and ERbeta function as a repressor in the osteogenic differentiation in *MSCs*. These results suggest that mouse *MSCs* are anabolic targets of estrogen action, via ERalpha activation. J. Cell. Biochem. Suppl. 36: 144-155, 2001.

...; Marrow Cells--metabolism--ME; Bone Marrow Cells--pathology--PA; Bone Morphogenetic Proteins--genetics--GE; Bone Morphogenetic Proteins --metabolism--ME; Cell Differentiation; Cell Division; Cells, Cultured; *Collagen*--genetics--GE; *Collagen*--metabolism--ME; Immunohistochemistry ; Mesoderm--pathology--PA; Mice; Ovariectomy; RNA, Messenger--metabolism --ME; Receptors, Estrogen--genetics--GE; Reverse Transcriptase Polymerase

Chain Reaction; Stem Cells--metabolism--ME...
...Chemical Name: RNA, Messenger; Receptors, Estrogen; Transcription Factors; Transforming Growth Factor beta; bone morphogenetic protein 2; estrogen receptor alpha; estrogen receptor beta; transforming growth factor beta1; Estradiol; *Collagen*; Alkaline Phosphatase

8/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11262348 21293154 PMID: 11400162
Fibromodulin is expressed by both chondrocytes and osteoblasts during fetal bone development.
Gori F; Schipani E; Demay M B
Endocrine Unit, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA.
Journal of cellular biochemistry (United States) Apr 2-27 2001, 82 (1) p46-57, ISSN 0730-2312 Journal Code: 8205768
Contract/Grant No.: 1 F32 DE-05754-01; DE; NIDCR; AR-44855; AR; NIAMS; DK36597; DK; NIDDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Fibromodulin, a keratan-sulfate proteoglycan, was first isolated in articular cartilage and tendons. We have identified fibromodulin as a gene regulated during *BMP*-*2* -induced differentiation of a mouse prechondroblastic cell line. Because expression of fibromodulin during endochondral *bone* *formation* has not been studied, we examined whether selected cells of the chondrocytic and osteoblastic lineage expressed fibromodulin. Fibromodulin mRNA was detected in conditionally immortalized murine *bone* *marrow* *stromal* *cells*, osteoblasts, and growth plate chondrocytes, as well as in primary murine calvarial osteoblasts. We, therefore, investigated the temporo-spatial expression of fibromodulin in vivo during endochondral *bone* *formation* by in situ hybridization. Fibromodulin was first detected at 15.5 days post coitus (dpc) in the perichondrium and proliferating chondrocytes. Fibromodulin mRNA was also...

... collar and periosteum. At later time points fibromodulin was expressed in the primary spongiosa and the endosteum. To determine whether fibromodulin was expressed during intramembranous *bone* *formation* as well, in situ hybridization was performed on calvariae. Fibromodulin mRNA was present in calvarial osteoblasts from 15.5 dpc. These results demonstrate that fibromodulin...

... cartilage and bone cells during endochondral and intramembranous ossification. These findings suggest that this extracellular matrix protein plays a role in both endochondral and intramembranous *bone* *formation*. Copyright 2001 Wiley-Liss, Inc.
...; Morphogenetic Proteins--pharmacology--PD; Bone and Bones--metabolism --ME; Carrier Proteins--drug effects--DE; Carrier Proteins--genetics--GE; Cartilage--metabolism--ME; Cell Line--metabolism--ME; *Collagen*--chemistry --CH; Extracellular Matrix Proteins--drug effects--DE; Extracellular Matrix Proteins--genetics--GE; Gene Expression; In Situ Hybridization --methods--MT; Mice; Osteocalcin--analysis--AN; RNA...
Chemical Name: Bone Morphogenetic Proteins; CBFA-1 transcription factor; Carrier Proteins; Extracellular Matrix Proteins; RNA, Messenger; Transcription Factors; bone morphogenetic protein 2; Osteocalcin; fibromodulin; *Collagen*
?ds

Set	Items	Description
S1	7094	(BONE (W) MARROW (W) STROMAL (W) CELL?) OR (MSC?)
S2	72	S1 (S) ((BMP-2) OR (BMP (W) 2))
S3	25	S2 AND (BONE (W) (FORMATION OR REPAIR))

```
S4          9   S3 AND (ALGINATE OR COLLAGEN OR POLYMER)
S5          3   S4 AND (ADENOVIRUS OR ADENOVIRAL)
S6          1   RD (unique items)
S7          4   RD S4 (unique items)
S8          3   S7 NOT S6
?rd s3
...completed examining records
      S9       10  RD S3 (unique items)
?s s9 not s7
              10  S9
               4  S7
     S10       6  S9 NOT S7
?t s10/3,k/all
```

10/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13317387 22040539 PMID: 12045254

Cyclooxygenase-2 regulates mesenchymal cell differentiation into the osteoblast lineage and is critically involved in *bone* *repair*.

Zhang Xinping; Schwarz Edward M; Young Donald A; Puzas J Edward; Rosier Randy N; O'Keefe Regis J

The Center for Musculoskeletal Research, University of Rochester Medical Center, New York 14642, USA.

Journal of clinical investigation (United States) Jun 2002, 109 (11) p1405-15, ISSN 0021-9738 Journal Code: 7802877

Contract/Grant No.: AR-45971; AR; NIAMS; AR-46545; AR; NIAMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Cyclooxygenase-2 regulates mesenchymal cell differentiation into the osteoblast lineage and is critically involved in *bone* *repair*.

Preclinical and clinical studies suggest a possible role for cyclooxygenases in *bone* *repair* and create concerns about the use of nonsteroidal antiinflammatory drugs in patients with skeletal injury. We utilized wild-type, COX-1(-/-), and COX-2(-/-) mice to demonstrate that COX-2 plays an essential role in both endochondral and intramembranous *bone* *formation* during skeletal repair. The healing of stabilized tibia fractures was significantly delayed in COX-2(-/-) mice compared with COX-1(-/-) and wild-type controls. The...

... of undifferentiated mesenchyme and a marked reduction in osteoblastogenesis that resulted in a high incidence of fibrous nonunion in the COX-2(-/-) mice. Similarly, intramembranous *bone* *formation* on the calvaria was reduced 60% in COX-2(-/-) mice following in vivo injection of FGF-1 compared with either COX-1(-/-) or wild-type mice. To elucidate the mechanism involved in reduced *bone* *formation*, osteoblastogenesis was studied in *bone* *marrow* *stromal* *cell* cultures obtained from COX-2(-/-) and wild-type mice. Bone nodule formation was reduced 50% in COX-2(-/-) mice. The defect in osteogenesis was completely rescued by addition of prostaglandin E2 (PGE(2)) to the cultures. In the presence of bone morphogenetic protein (*BMP*-*2*), bone nodule formation was enhanced to a similar level above that observed with PGE(2) alone in both control and COX-2(-/-) cultures, indicating that...

... of prostaglandins. Furthermore, we found that the defect in COX-2(-/-) cultures correlated with significantly reduced levels of cbfa1 and osterix, two genes necessary for *bone* *formation*. Addition of PGE(2) rescued this defect, while *BMP*-*2* enhanced cbfa1 and osterix in both COX-2(-/-) and wild-type cultures. Finally, the effects of these agents were additive, indicating that COX-2 is...

10/3,K/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

11203153 21221271 PMID: 11319905

Exogenously regulated stem cell-mediated gene therapy for bone regeneration.

Moutsatsos I K; Turgeman G; Zhou S; Kurkalli B G; Pelled G; Tzur L; Kelley P; Stumm N; Mi S; Muller R; Zilberman Y; Gazit D

Molecular Pathology Laboratory, Hebrew University-Hadassah Medical and Gene Therapy Center, Jerusalem, Israel.

Molecular therapy : the journal of the American Society of Gene Therapy (United States) Apr 2001, 3 (4) p449-61, ISSN 1525-0016

Journal Code: 100890581

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

... monitor and control complex biological processes. We report here a regulated stem cell-based system for controlling bone regeneration, utilizing genetically engineered mesenchymal stem cells (*MSCs*) harboring a tetracycline-regulated expression vector encoding the osteogenic growth factor human *BMP*-*2*. We show that doxycycline (a tetracycline analogue) is able to control hBMP-2 expression and thus control *MSC* osteogenic differentiation both in vitro and in vivo. Following in vivo transplantation of genetically engineered *MSCs* , doxycycline administration controlled both *bone* *formation* and bone regeneration. Moreover, our findings showed increased angiogenesis accompanied by *bone* *formation* whenever genetically engineered *MSCs* were induced to express hBMP-2 in vivo. Thus, our results demonstrate that regulated gene expression in mesenchymal stem cells can be used as a...

10/3,K/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10363654 99359866 PMID: 10430653

Regulation of osteogenic differentiation of human bone marrow stromal cells: interaction between transforming growth factor-beta and 1,25(OH)(2) vitamin D(3) In vitro.

Liu P; Oyajobi B O; Russell R G; Scutt A

Human Metabolism and Clinical Biochemistry, Division of Biochemical and Musculoskeletal Medicine, University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX, Great Britain.

Calcified tissue international (UNITED STATES) Aug 1999, 65 (2) p173-80, ISSN 0171-967X Journal Code: 7905481

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Bone *marrow* *stromal* *cells* are believed to play a major role in *bone* *formation* as a major source of osteoprogenitor cells, however, very little is known about how the osteogenic differentiation of these cells is regulated by systemic hormones...

... beta and its interaction with 1, 25(OH)(2) Vitamin D(3) [1,25(OH)(2)D(3)] on the differentiation and proliferation of human *bone* *marrow* *stromal* *cells* (hBMSC) in secondary cultures. Alkaline phosphatase (ALP) activity was inhibited by TGF-beta (0.1-10 ng/ml) and increased by 1, 25(OH)(2...

... effect on hBMSC proliferation. As no synergistic effect was seen with combinations of 1,25(OH)(2)D(3) and other osteotrophic growth factors, including *BMP*-*2* , IGF-I, and basic fibroblast growth factor (bFGF), it would seem likely that the synergistic interaction is specific for TGF-beta. The increased ALP activity...

10/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09576209 97472251 PMID: 9333121

Stimulatory effects of basic fibroblast growth factor and bone morphogenetic protein-2 on osteogenic differentiation of rat bone marrow-derived mesenchymal stem cells.

Hanada K; Dennis J E; Caplan A I
Skeletal Research Center, Department of Biology, Case Western Reserve University, Cleveland, Ohio, U.S.A.

Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research (UNITED STATES) Oct 1997, 12 (10) p1606-14, ISSN 0884-0431 Journal Code: 8610640
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Bone marrow stroma contains multipotential mesenchymal progenitor cells which can differentiate into osteoblastic cells; we refer to these cells as mesenchymal stem cells (*MSCs*). Basic fibroblast growth factor (bFGF) and bone morphogenetic protein-2 (*BMP*-*2*) have been implicated in the osteogenic regulatory process by virtue of their mitogenic and differentiation activities, respectively. This study examines and compares the effects of bFGF and *BMP*-*2* on dexamethasone (Dex)-dependent in vitro osteogenic differentiation of rat marrow-derived *MSCs*. A 6-day exposure to bFGF markedly stimulated cell growth and induced osteoblastic differentiation as shown by osteocalcin mRNA expression (day 14), bone nodule formation (day 18), and calcium deposition (day 18). These results indicate that bFGF enhances both mitogenic activity and osteogenic development of Dex-treated marrow *MSCs*. In contrast, *BMP*-*2* did not induce osteogenesis as strongly as bFGF. Thus, exposure to *BMP*-*2* slightly increased bone nodule number and calcium content compared with the control. Exposure of *MSCs* to both *BMP*-*2* and bFGF induced expression of osteocalcin mRNA and mineralizing bone-like nodules as early as day 11 and resulted in enhancement of *bone* *formation* more markedly than either factor alone. Consistent with these results, porous calcium phosphate ceramic cubes implanted in vivo, which were loaded with *MSCs* pre-exposed to both bFGF and *BMP*-*2*, showed higher histologic score for *bone* *formation* than those with *MSCs* pre-exposed to either bFGF or *BMP*-*2* alone. These data indicate that combined treatment with bFGF and *BMP*-*2* synergistically enhances the osteogenic potency of bFGF in rat marrow *MSC* culture.

10/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09440586 97345731 PMID: 9202223

Glucocorticoid-induced differentiation of fetal rat calvarial osteoblasts is mediated by bone morphogenetic protein-6.

Boden S D; Hair G; Titus L; Racine M; McCuaig K; Wozney J M; Nanes M S
Department of Orthopaedic Surgery, Emory University School of Medicine and Veterans Affairs Medical Center, Atlanta, Georgia 30033, USA.

Endocrinology (UNITED STATES) Jul 1997, 138 (7) p2820-8, ISSN 0013-7227 Journal Code: 0375040
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Glucocorticoids (GCs) at physiological concentrations promote osteoblast differentiation from fetal calvarial cells, calvarial organ cultures, and *bone* *marrow* *stromal* *cells*; however, the cellular pathways involved

are not known. Bone morphogenetic proteins (BMPs) are recognized as important mediators of osteoblast differentiation. Specific roles for individual BMPs during postembryonic membranous *bone* *formation* have yet to be determined. We recently reported that GC potentiated the osteoblast differentiation effects of *BMP*-*2* and BMP-4, but not of BMP-6, which, by itself, was the most potent of the three. In the present study, we used fetal...

10/3,K/6 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

07778893 EMBASE No: 1999261743
Regulation of osteogenic differentiation of human bone marrow stromal cells: Interaction between transforming growth factor-beta and 1,25(OH)inf 2 Vitamin Dinf 3 in vitro
Liu P.; Oyajobi B.O.; Russell R.G.G.; Scutt A.
A. Scutt, Human Metabolism/Clin. Biochemistry, Biochem./Musculoskeletal Med. Div., University of Sheffield Medical Sch., Beech Hill Road, Sheffield S10 2RX United Kingdom
Calcified Tissue International (CALCIF. TISSUE INT.) (United States) 1999, 65/2 (173-180)
CODEN: CTIND ISSN: 0171-967X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 45

Bone *marrow* *stromal* *cells* are believed to play a major role in *bone* *formation* as a major source of osteoprogenitor cells, however, very little is known about how the osteogenic differentiation of these cells is regulated by systemic hormones...

...and its interaction with 1,25(OH)inf 2 Vitamin Dinf 3 [1,25(OH)inf 2Dinf 3] on the differentiation and proliferation of human *bone* *marrow* *stromal* *cells* (hBMSC) in secondary cultures. Alkaline phosphatase (ALP) activity was inhibited by TGF-beta (0.1-10 ng/ml) and increased by 1,25(OH)inf...

...effect on hBMSC proliferation. As no synergistic effect was seen with combinations of 1,25(OH)inf 2Dinf 3 and other osteotrophic growth factors, including *BMP*-*2*, IGF- I, and basic fibroblast growth factor (bFGF), it would seem likely that the synergistic interaction is specific for TGF-beta. The increased ALP activity...
?ds

Set	Items	Description
S1	7094	(BONE (W) MARROW (W) STROMAL (W) CELL?) OR (MSC?)
S2	72	S1 (S) ((BMP-2) OR (BMP (W) 2))
S3	25	S2 AND (BONE (W) (FORMATION OR REPAIR))
S4	9	S3 AND (ALGINATE OR COLLAGEN OR POLYMER)
S5	3	S4 AND (ADENOVIRUS OR ADENOVIRAL)
S6	1	RD (unique items)
S7	4	RD S4 (unique items)
S8	3	S7 NOT S6
S9	10	RD S3 (unique items)
S10	6	S9 NOT S7

```
?s s1 and ((BMP-2) or (BMP (w) 2))
          7094  S1
            86  BMP-2
          7797  BMP
       7451944  2
          2258  BMP(W)2
    S11     83  S1 AND ((BMP-2) OR (BMP (W) 2))
?s s11 and (polymer or collagen or alginate)
            83  S11
```

```
          80771  POLYMER
         239662  COLLAGEN
          11747  ALGINATE
     S12     26  S11 AND (POLYMER OR COLLAGEN OR ALGINATE)
?s s12 and (implant or transplant or repair or (bone (w) formation))
             26  S12
          85768  IMPLANT
         145683  TRANSPLANT
         236099  REPAIR
         962016  BONE
        1159611  FORMATION
          27294  BONE(W)FORMATION
     S13      9  S12 AND (IMPLANT OR TRANSPLANT OR REPAIR OR (BONE (W)
                 FORMATION))
?rd
...completed examining records
     S14      4  RD (unique items)
?t s14/3,k/all
```

14/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12710055 21588136 PMID: 11551928

Cloning and characterization of a novel WD-40 repeat protein that dramatically accelerates osteoblastic differentiation.

Gori F; Divieti P; Demay M B
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Record type: Completed

The bone morphogenetic proteins (BMPs) play a pivotal role in endochondral *bone* *formation* . Using differential display polymerase chain reaction, we have identified a novel gene, named BIG-3 (*BMP*-*2* -induced gene 3 kb), that is induced as a murine prechondroblastic cell line, MLB13MYC clone 17, acquires osteoblastic features in response to *BMP*-*2* treatment. The 3-kilobase mRNA encodes a 34-kDa protein containing seven WD-40 repeats. Northern and Western analyses demonstrated that BIG-3 mRNA and protein were induced after 24 h of *BMP*-*2* treatment. BIG-3 mRNA was expressed in conditionally immortalized murine *bone* *marrow* *stromal* *cells* , osteoblasts, osteocytes, and growth plate chondrocytes, as well as in primary calvarial osteoblasts. Immunohistochemistry demonstrated that BIG-3 was expressed in the osteoblasts of calvariae...

...clones. This increase in cAMP production was associated with an increase in PTH binding. Expression of BIG-3 increased mRNA levels encoding Cbfa1, type I *collagen*, and osteocalcin and accelerated formation of mineralized nodules. In conclusion, we have identified a novel WD-40 protein, induced by *BMP*-*2* treatment, that dramatically accelerates the program of osteoblastic differentiation in stably transfected MC3T3E1 cells.

14/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11282430 21348043 PMID: 11455579

Estrogen modulates estrogen receptor alpha and beta expression, osteogenic activity, and apoptosis in mesenchymal stem cells (*MSCs*) of osteoporotic mice.

Zhou S; Zilberman Y; Wassermann K; Bain S D; Sadovsky Y; [redacted]azit D
Molecular Pathology Laboratory, Hebrew University-Hadassah Medical and Gene Therapy Center, Jerusalem 91120, Israel.
Journal of cellular biochemistry (United States) 2001, Suppl 36 p144-55, ISSN 0730-2312 Journal Code: 8205768
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Estrogen modulates estrogen receptor alpha and beta expression, osteogenic activity, and apoptosis in mesenchymal stem cells (*MSCs*) of osteoporotic mice.

...mouse, ovariectomy (OVX) leads to significant reductions in cancellous bone volume while estrogen (17beta-estradiol, E2) replacement not only prevents bone loss but can increase *bone* *formation*. As the E2-dependent increase in *bone* *formation* would require the proliferation and differentiation of osteoblast precursors, we hypothesized that E2 regulates mesenchymal stem cells (*MSCs*) activity in mouse bone marrow. We therefore investigated proliferation, differentiation, apoptosis, and estrogen receptor (ER) alpha and beta expression of primary culture *MSCs* isolated from OVX and sham-operated mice. *MSCs*, treated in vitro with 10(-7) M E2, displayed a significant increase in ERalpha mRNA and protein expression as well as alkaline phosphatase (ALP) activity...

... mRNA and protein expression as well as apoptosis in both OVX and sham mice. E2 up-regulated the mRNA expression of osteogenic genes for ALP, *collagen* I, TGF-beta1, *BMP*-*2*, and cbfa1 in *MSCs*. In a comparison of the relative mRNA expression and protein levels for two ER isoforms, ERalpha was the predominant form expressed in *MSCs* obtained from both OVX and sham-operated mice. Cumulatively, these results indicate that estrogen in vitro directly augments the proliferation and differentiation, ERalpha expression, osteogenic gene expression and, inhibits apoptosis and ERbeta expression in *MSCs* obtained from OVX and sham-operated mice. Co-expression of ERalpha, but not ERbeta, and osteogenic differentiation markers might indicate that ERalpha function as an activator and ERbeta function as a repressor in the osteogenic differentiation in *MSCs*. These results suggest that mouse *MSCs* are anabolic targets of estrogen action, via ERalpha activation. J. Cell. Biochem. Suppl. 36: 144-155, 2001. Copyright 2001 Wiley-Liss, Inc.

...; Marrow Cells--metabolism--ME; Bone Marrow Cells--pathology--PA; Bone Morphogenetic Proteins--genetics--GE; Bone Morphogenetic Proteins --metabolism--ME; Cell Differentiation; Cell Division; Cells, Cultured; *Collagen*--genetics--GE; *Collagen*--metabolism--ME; Immunohistochemistry ; Mesoderm--pathology--PA; Mice; Ovariectomy; RNA, Messenger--metabolism --ME; Receptors, Estrogen--genetics--GE; Reverse Transcriptase Polymerase Chain Reaction; Stem Cells--metabolism--ME...

...Chemical Name: RNA, Messenger; Receptors, Estrogen; Transcription Factors; Transforming Growth Factor beta; bone morphogenetic protein 2; estrogen receptor alpha; estrogen receptor beta; transforming growth factor beta1; Estradiol; *Collagen*; Alkaline Phosphatase

14/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11262348 21293154 PMID: 11400162

Fibromodulin is expressed by both chondrocytes and osteoblasts during fetal bone development.

Gori F; Schipani E; Demay M B
Endocrine Unit, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA.
Journal of cellular biochemistry (United States) Apr 2-27 2001, 82 (1) p46-57, ISSN 0730-2312 Journal Code: 8205768
Contract/Grant No.: 1 F32 DE-05754-01; DE; NIDCR; AR-44855; AR; NIAMS; DK36597; DK; NIDDK

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Fibromodulin, a keratan-sulfate proteoglycan, was first isolated in articular cartilage and tendons. We have identified fibromodulin as a gene regulated during *BMP*-*2* -induced differentiation of a mouse prechondroblastic cell line. Because expression of fibromodulin during endochondral *bone* *formation* has not been studied, we examined whether selected cells of the chondrocytic and osteoblastic lineage expressed fibromodulin. Fibromodulin mRNA was detected in conditionally immortalized murine *bone* *marrow* *stromal* *cells*, osteoblasts, and growth plate chondrocytes, as well as in primary murine calvarial osteoblasts. We, therefore, investigated the temporo-spatial expression of fibromodulin in vivo during endochondral *bone* *formation* by in situ hybridization. Fibromodulin was first detected at 15.5 days post coitus (dpc) in the perichondrium and proliferating chondrocytes. Fibromodulin mRNA was also...

... collar and periosteum. At later time points fibromodulin was expressed in the primary spongiosa and the endosteum. To determine whether fibromodulin was expressed during intramembranous *bone* *formation* as well, in situ hybridization was performed on calvariae. Fibromodulin mRNA was present in calvarial osteoblasts from 15.5 dpc. These results demonstrate that fibromodulin...

... cartilage and bone cells during endochondral and intramembranous ossification. These findings suggest that this extracellular matrix protein plays a role in both endochondral and intramembranous *bone* *formation*.

...; Morphogenetic Proteins--pharmacology--PD; Bone and Bones--metabolism --ME; Carrier Proteins--drug effects--DE; Carrier Proteins--genetics--GE; Cartilage--metabolism--ME; Cell Line--metabolism--ME; *Collagen*--chemistry --CH; Extracellular Matrix Proteins--drug effects--DE; Extracellular Matrix Proteins--genetics--GE; Gene Expression; In Situ Hybridization --methods--MT; Mice; Osteocalcin--analysis--AN; RNA...
Chemical Name: Bone Morphogenetic Proteins; CBFA-1 transcription factor; Carrier Proteins; Extracellular Matrix Proteins; RNA, Messenger; Transcription Factors; bone morphogenetic protein 2; Osteocalcin; fibromodulin; *Collagen*

14/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11180690 21205495 PMID: 11310352
In vitro and in vivo induction of *bone* *formation* using a recombinant adenoviral vector carrying the human *BMP*-*2* gene.
Cheng S L; Lou J; Wright N M; Lai C F; Avioli L V; Riew K D
Division of Bone and Mineral Diseases, Dept. of Internal Medicine, Washington University School of Medicine, St. Louis, Missouri, USA.
Calcified tissue international (United States) Feb 2001, 68 (2) p87-94, ISSN 0171-967X Journal Code: 7905481
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

In vitro and in vivo induction of *bone* *formation* using a recombinant adenoviral vector carrying the human *BMP*-*2* gene.
It has been well established that bone morphogenetic protein-2 (*BMP*-*2*) can induce *bone* *formation* both in vivo and in vitro, although high concentrations (up to milligrams) of *BMP*-*2* have been required to achieve this effect in vivo. Further, clinical applications are usually limited to a single dose at the time of implantation. In an attempt to prolong the transforming effect of *BMP*-*2* we used a recombinant

adenoviral vector carrying the human *BMP*-*2* gene (Adv-B[redacted]2) to transduce marrow-derived mesenchymal stem cells (*MSC*) of skeletally mature male New Zealand white rabbits. The pluripotential *MSC* were incubated with Adv-BMP2 overnight followed by culture in growth medium for 1 week. Assays on tissue cultures demonstrated that these Adv-BMP2 transduced *MSC* produced *BMP*-*2* protein, differentiated into an osteoprogenitor line, and induced *bone* *formation* in vitro. These *MSC* had increased alkaline phosphatase activity, increased expression of type I *collagen* , osteopontin, and osteocalcin mRNA, and induced matrix mineralization compared with both non-transduced cells and cells transduced with a control adenoviral construct. To analyze the osteogenic potential in vivo, Adv-BMP2-transduced *MSC* were autologously implanted into the intertransverse process space between L5 and L6 of the donor rabbits. The production of new bone was demonstrated by radiographic...

... BMP2, whereas no bone was evident at sites implanted with cells transduced with the control adenoviral construct. Histological examination further confirmed the presence of new *bone* *formation*. These accumulated data indicate that it is possible to successfully transduce mesenchymal stem cells with a recombinant adenoviral vector carrying the gene for *BMP* -*2* such that these cells will produce *BMP*-*2*, differentiate into an osteoprogenitor line, and induce *bone* *formation* both in vitro and in vivo. Moreover, incubation of the Adv-BMP2-transduced cells for an additional 7 days in culture before transplantation enhances the success rate in *bone* *formation* (three out of three) as compared with our previous report (one out of five, Calcif Tissue Int 63:357-360, 1998).
...; Bone Marrow Cells--cytology--CY; Bone Marrow Cells--drug effects --DE; Bone Marrow Cells--metabolism--ME; Cell Differentiation --drug effects--DE; Cell Transplantation; Cells, Cultured; *Collagen* --biosynthesis--BI; *Collagen*--genetics--GE; Genetic Vectors; Lumbar Vertebrae--surgery--SU; Models, Animal; Osteocalcin--biosynthesis--BI; Osteocalcin--genetics--GE; RNA, Messenger--metabolism--ME; Rabbits; Sialoglycoproteins--biosynthesis--BI; Sialoglycoproteins...
Chemical Name: Bone Morphogenetic Proteins; Genetic Vectors; RNA, Messenger; Sialoglycoproteins; bone morphogenetic protein 2; Osteocalcin; osteopontin; *Collagen*; Alkaline Phosphatase
?ds

Set	Items	Description
S1	7094	(BONE (W) MARROW (W) STROMAL (W) CELL?) OR (MSC?)
S2	72	S1 (S) ((BMP-2) OR (BMP (W) 2))
S3	25	S2 AND (BONE (W) (FORMATION OR REPAIR))
S4	9	S3 AND (ALGINATE OR COLLAGEN OR POLYMER)
S5	3	S4 AND (ADENOVIRUS OR ADENOVIRAL)
S6	1	RD (unique items)
S7	4	RD S4 (unique items)
S8	3	S7 NOT S6
S9	10	RD S3 (unique items)
S10	6	S9 NOT S7
S11	83	S1 AND ((BMP-2) OR (BMP (W) 2))
S12	26	S11 AND (POLYMER OR COLLAGEN OR ALGINATE)
S13	9	S12 AND (IMPLANT OR TRANSPLANT OR REPAIR OR (BONE (W) FORMATION))
S14	4	RD (unique items)

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$2.73 13 Types
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$7.95 Estimated cost File5
$18.54 2.060 DialUnits File73
$2.50 1 Type(s) in Format 3
$2.50 1 Types
$21.04 Estimated cost File73

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  $2.16 TELNET
 $38.65 Estimated cost this search
 $38.99 Estimated total session cost   5.056 DialUnits


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Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND		
L7	L6 and (bone adj (defect or repair))	12	L7
L6	L2 same ((BMP adj 2) or (BMP-2))	18	L6
L5	L4 and (alginate or polymer or collagen)	31	L5
L4	L3 and (adenovirus or (adenoviral adj vector))	32	L4
L3	L2 and (BMP-2)	64	L3
L2	((bone adj marrow) adj (stromal adj cell)) or (MSC)	7632	L2
L1	Chang-chia-Ning.in.	0	L1

END OF SEARCH HISTORY